INTRODUCTION

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The term "nonspecific resistance" is used in this Symposium to indicate defense reactions in which participation of specific antibody is not a requirement although antibody may enhance them greatly. In the unimmunized host the various nonspecific mechanisms are the primary defenses, with specific antibody playing a secondary role because of the delay in its production. In the most acute infections of normal man and animals, death or survival may be almost entirely dependent upon nonspecific mechanisms for the reason that overwhelming microbial multiplication can occur during a period so short that in the immunologically inexperienced animal effective quantities of protective antibody, whether opsonic or antitoxic, cannot be produced quickly enough. Indeed, the innate susceptibility (or resistance) of an animal species or strain thereof may be most simply considered as the capacity of its nonspecific mechanisms, both cellular and humoral, to cope with particular microbial agents. In the case of highly virulent microbes with a short generation time, the outcome will be decided within a relatively brief period following infection, whereas with agents of lower virulence or with those that have a long generation time, the decision will be correspondingly delayed.

The limitations of active immunization by artificial means are many. Among them may be cited the diversity of specific antigens that must be considered, the difficulties in preparing adequate amounts of stable antigens in sufficient purity for widescale use, and the length of time required for the development of immunity, even granting that the formidable logistic problems of preparation and application can be solved. Although specific active immunization has proved its usefulness in many instances, its application on a general scale, employing a variety of antigens, requires that the benefits to be achieved are immediately apparent, as in the prevention of acute bacterial and viral infections of childhood, prevention of dire consequences to the general population as in the case of epidemic influenza, or under military circumstances.

Because of these limitations it is worthwhile to seek means to enhance the activity of nonspecific cellular and humoral factors so that the infectious process may be contained by them or else that sufficient time can be bought so that specific active immunity can come into the picture. None of the papers in this Symposium hold out much promise that with present knowledge such ends can be achieved. Nonetheless, in view of the revival of interest in the study of the pathogenesis of infections and the natural mechanisms of resistance to them, the outlook is a bit brighter. A few interesting leads have been turned up in recent years such as the effect of endotoxins of gram-negative bacteria upon resistance, the activity of a dietary constituent in protecting mice against the effects of natural infection by *Salmonella*, and of considerable significance, the resistance of agammaglobulinemic children to certain viral infections, but great susceptibility to viral hepatitis and to most bacterial infections.

Some important aspects of nonspecific resistance received little or no attention in the Symposium. For instance, factors pertaining to surfaces—the skin and mucous membranes—were not considered, nor was the role of lymphatic blockade. A research area of the greatest significance, namely genetic constitution and resistance to infection, was the subject of only a single brief communication. It is reasonable to think that study of different inbred strains of animals will define genetically determined phenotypic characters that influence resistance or susceptibility. Present information indicates, as perhaps might have been anticipated, that inherited resistance is relatively specific in that it functions only against certain related infections and is not applicable to resistance in general. To enhance nonspecific resistance to a variety of unrelated agents by artificial means would imply, therefore, that a number of modifications will have to be induced in the host. If this view is correct, the chances of finding a single agent capable of causing a general enhancement of resistance appear to be slim.